Figure 1.

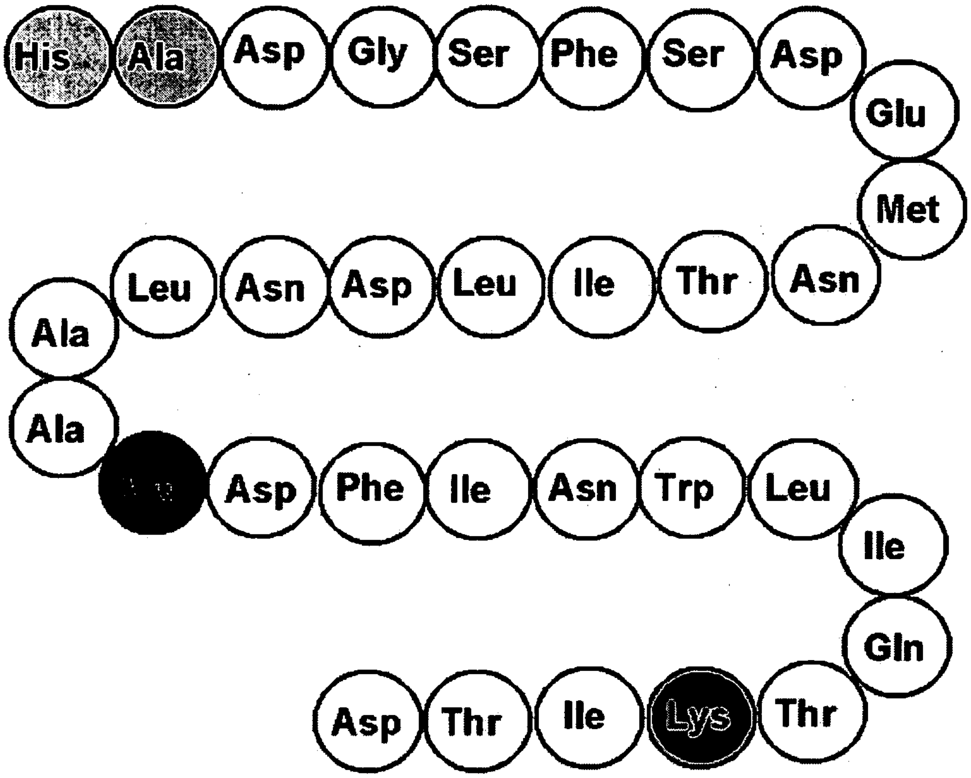

His
Ala
Asp
Gly
Ser
Phe
Ser
Asp
Glu
Met
Asn
Thr
Ile
Leu
Asp
Asn
Leu
Ala
Ala
Asp
Phe
Ile
Asn
Trp
Leu
Ile
Gln
Thr
Lys
Ile
Thr
Asp

Figure 2.

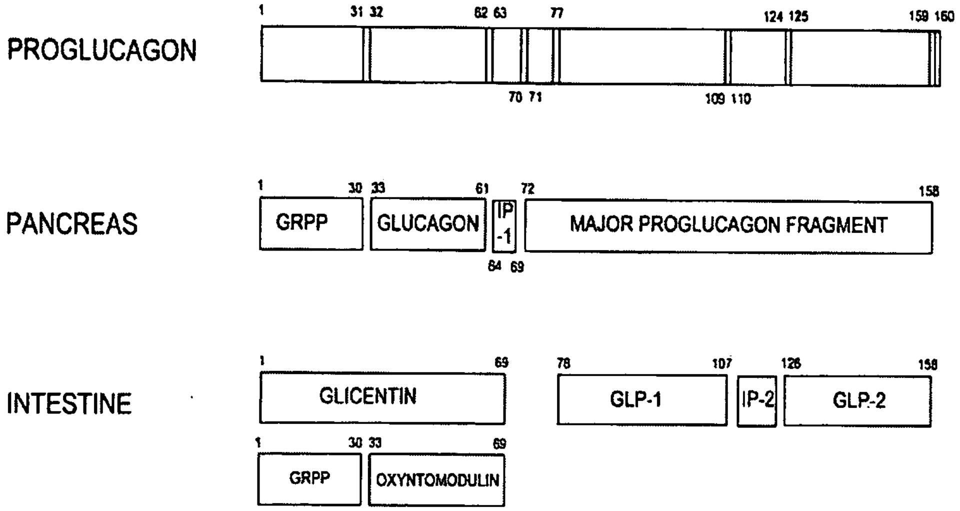

PROGLUCAGON
1
31 32
62 63
77
124 125
159 160
70 71
109 110
PANCREAS
1
30 33
61
72
158
GRPP
GLUCAGON
IP
-1
MAJOR PROGLUCAGON FRAGMENT
64 69
INTESTINE
1
69
78
107
126
158
GLICENTIN
GLP-1
IP-2
GLP-2
1
30 33
69
GRPP
OXYNTOMODULIN

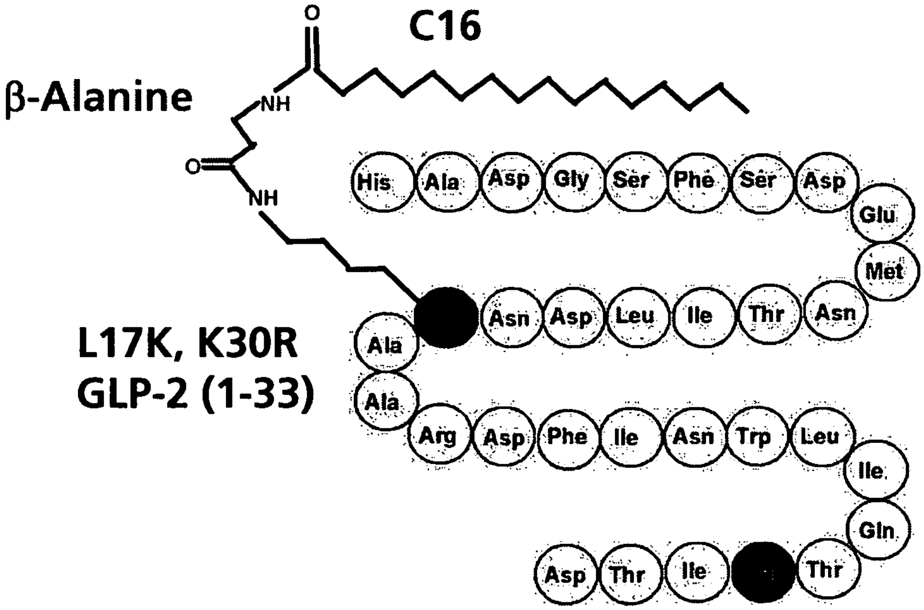
Figure 3.

Source	GLP-2 sequence	Accession no./ Ref. no.
Human	HADGSFSDEMNTILDNLAARDFINWLIQTKITD	P01275
Golden hamster	HADGSFSDEMNTILDSLATRDFINWLIQTKITD	P0127
Rat	HADGSFSDEMNTILDNLATRDFINWLIQTKITD	P06883
Guinea-pig	HADGSFSDEMNTILDNLATRDFINWLIQTKITD	P05110
Mouse	HADGSFSDEMSTILDNLATRDFINWLIQTKITD	P55095
Bovine	HADGSFSDEMNTVLDSLATRDFINWLLQTKITD	P01272
Pig	HADGSFSDEMNTVLDNLATRDFINWLLHTKITD	P01274
Degu (rodent)	HADGSFSDEMNTVLDHLATKDFINWLIQTKITD	P22890
Chicken	HADGTFTSDINKILDDMAAKEFLKWLINTKVTQ	I51301
Frog	HADGSFTSDFNKALDIKAAQEFLDWIINTPVKE	Ref. 37
Salamander	HADGSFTSDINKVLDTIAAKEFLNWLISTKVTE	AAB37529
Trout	HVDGSFTSDVNKVLDSLAAKEYLLWVMTSKTSG	Ref. 37

Figure 4.

Tissue	Fl quantitation, copies per µg total RNA	β-Actin quantitation, copies per µg total RNA	GLP-2R/-actin, ratio
Jejunum	11,900	15,500,000	76.8×10^{-5}
Duodenum	9,150	85,700,000	10.7×10^{-5}
Ileum	7,490	51,400,000	14.6×10^{-5}
Colon	4,150	19,800,000	21.0×10^{-5}
Stomach	1,530	23,600,000	6.48×10^{-5}
Brain	<600	40,600,000	$<1.48 \times 10^{-5}$
Heart	<600	6,600,000	$<9.09 \times 10^{-5}$
Kidney	<600	14,900,000	$<4.03 \times 10^{-5}$
Liver	<600	16,700,000	$<3.59 \times 10^{-5}$
Lung	<600	38,500,000	$<1.56 \times 10^{-5}$
Muscle	<600	4,600,000	$<13.0 \times 10^{-5}$
Spleen	<600	44,800,000	$<1.34 \times 10^{-5}$

Figure 5.

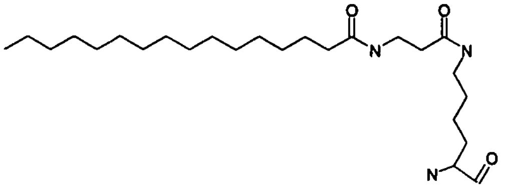

C16
β-Alanine
O
NH
O
NH
L17K, K30R
GLP-2 (1-33)
His
Ala
Asp
Gly
Ser
Phe
Ser
Asp
Glu
Met
Asn
Thr
Ile
Leu
Asp
Asn
Ala
Ala
Arg
Asp
Phe
Ile
Asn
Trp
Leu
Ile
Gln
Thr
Ile
Thr
Asp

6/12

Figure 6.

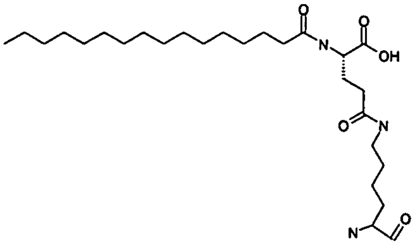
a) Example of the use of a β-alanine spacer on a lysine residue:

Lys(3-(hexadecanoylamino)propionyl):



b) Example of the use of a γ-glutamic acid spacer on a lysine residue:

Lys((S)-4-carboxy-4-(hexadecanoylamino)butanoyl):



c) Example of the use of a GABA spacer on a lysine residue:

Lys(4-(hexadecanoylamino)butanoyl):

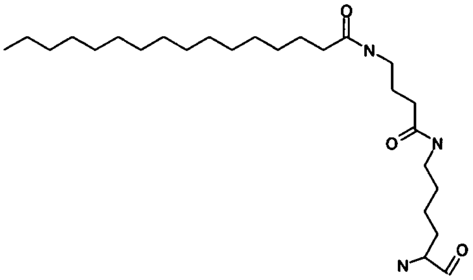


Figure 7.

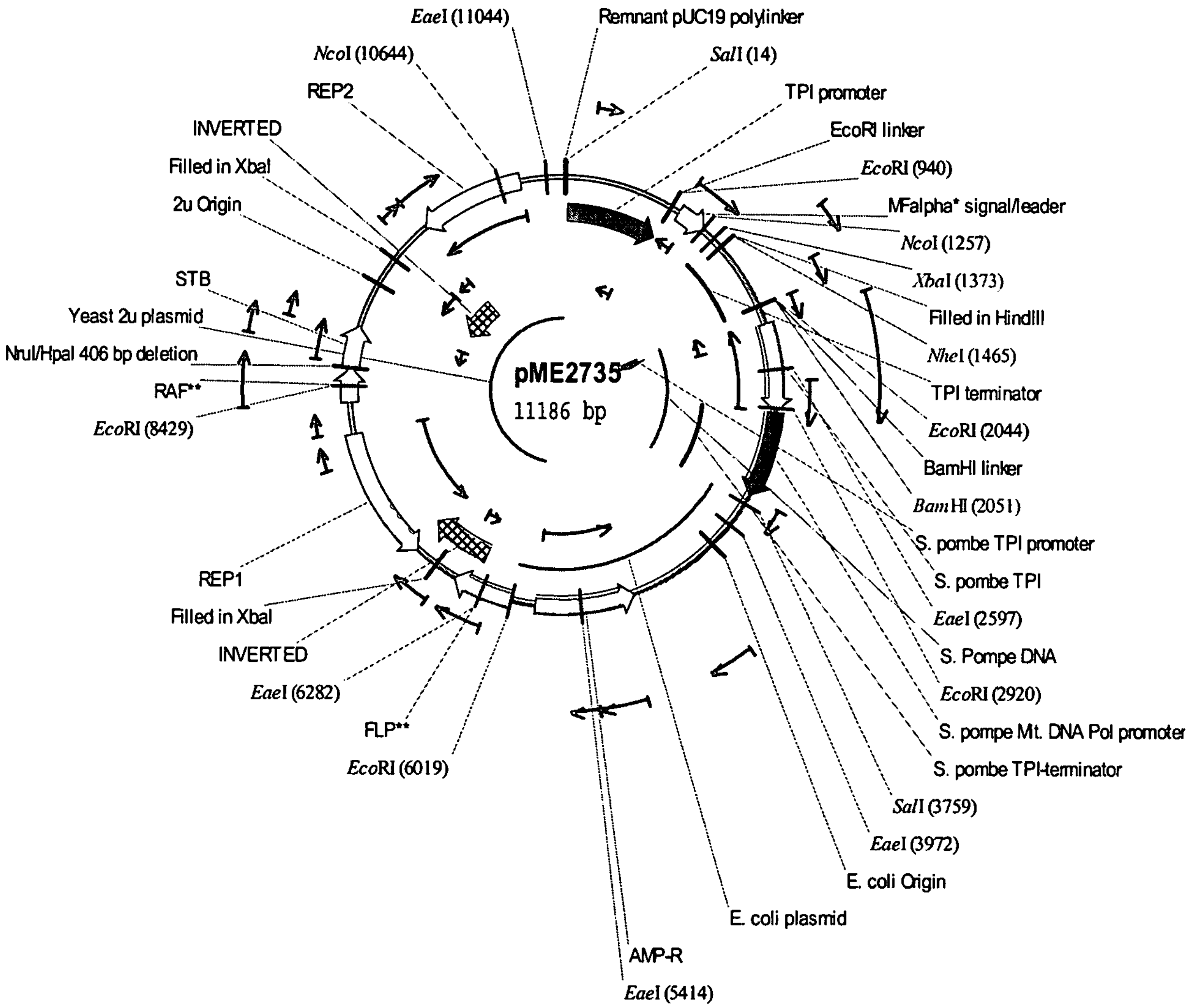

EaeI (11044)
Remnant pUC19 polylinker
NcoI (10644)
SalI (14)
REP2
TPI promoter
INVERTED
EcoRI linker
Filled in XbaI
EcoRI (940)
2u Origin
MFalpha* signal/leader
NcoI (1257)
XbaI (1373)
STB
Filled in HindIII
Yeast 2u plasmid
NheI (1465)
NruI/HpaI 406 bp deletion
TPI terminator
RAF**
EcoRI (8429)
EcoRI (2044)
BamHI linker
BamHI (2051)
S. pombe TPI promoter
S. pombe TPI
EaeI (2597)
S. Pompe DNA
EcoRI (2920)
S. pompe Mt. DNA Pol promoter
S. pombe TPI-terminator
SalI (3759)
EaeI (3972)
E. coli Origin
E. coli plasmid
AMP-R
EaeI (5414)
REP1
Filled in XbaI
INVERTED
EaeI (6282)
FLP**
EcoRI (6019)
pME2735
11186 bp

Figure 8.

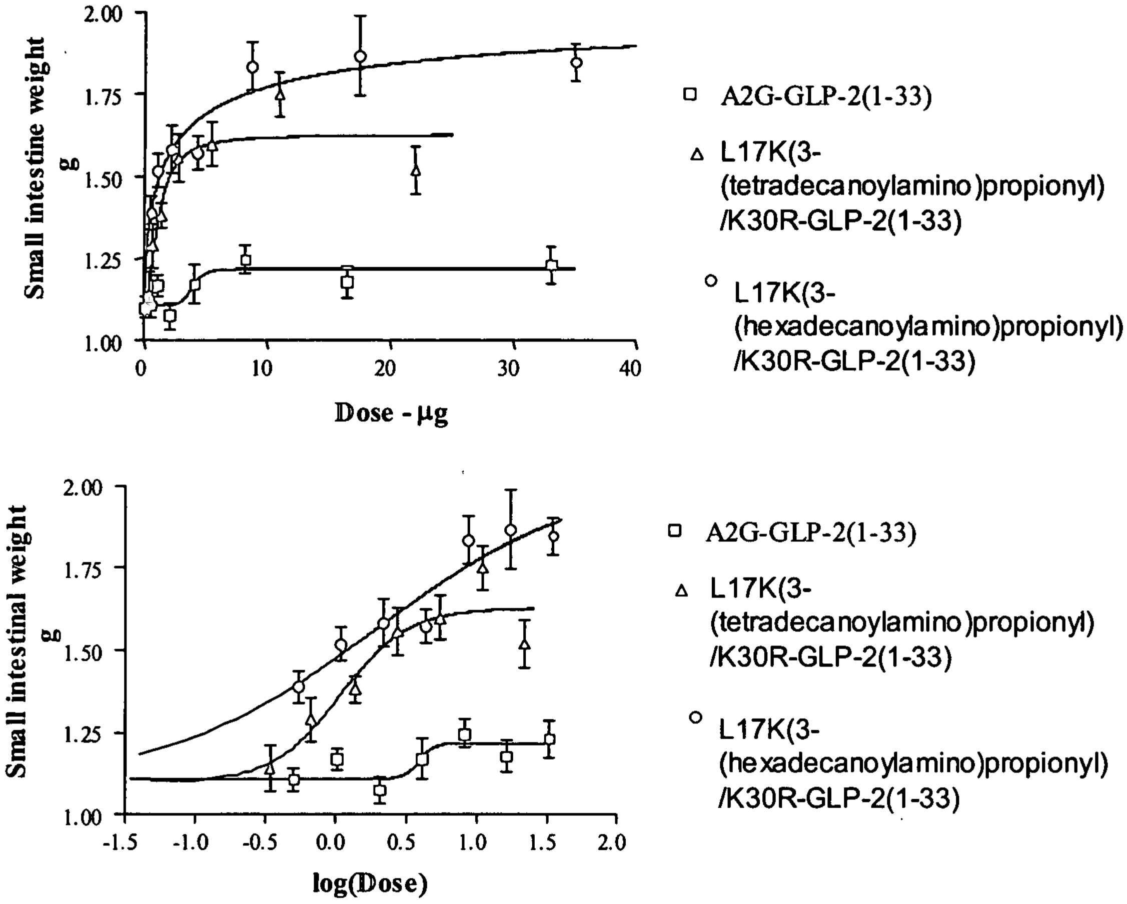
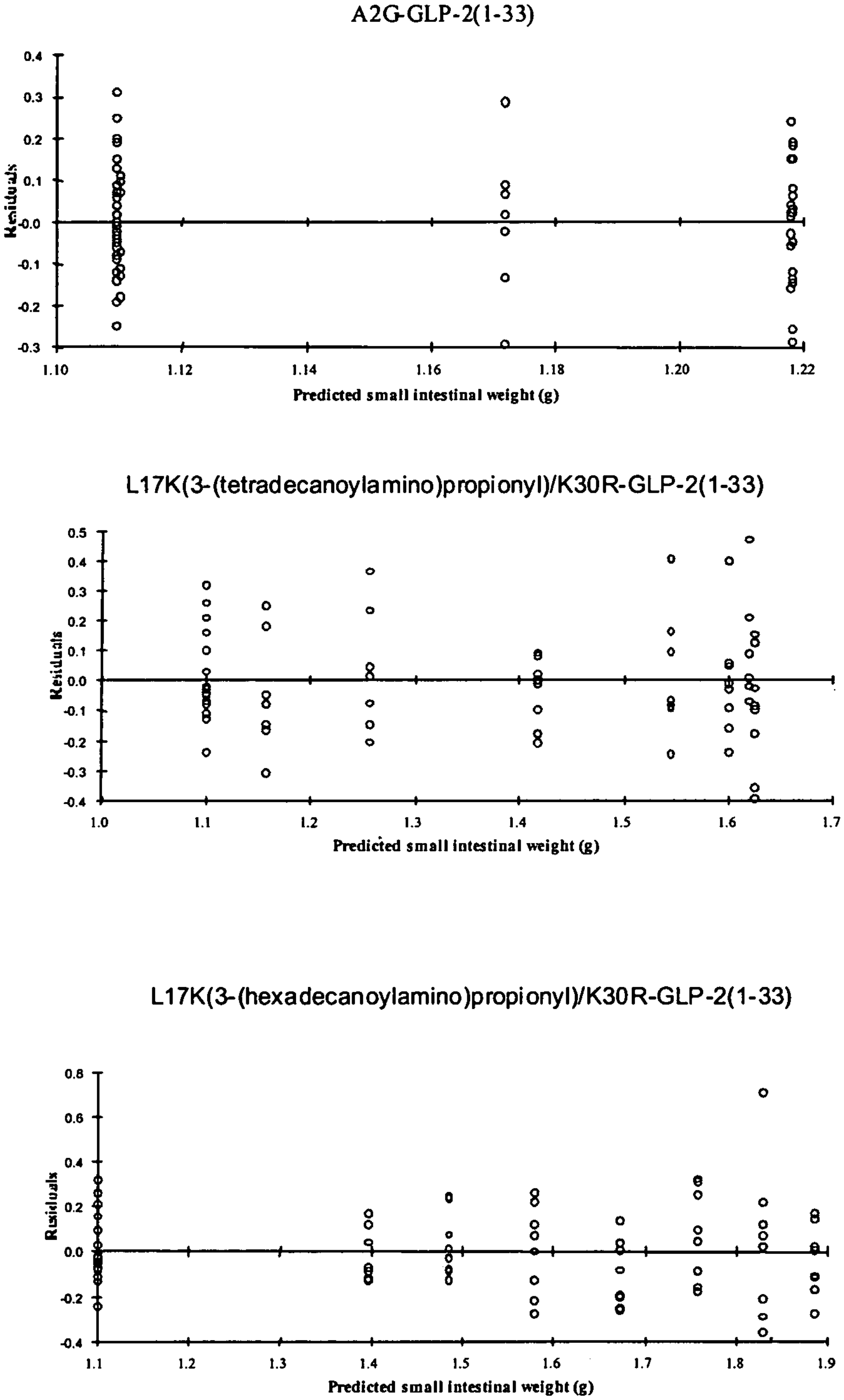

2.00
1.75
1.50
1.25
1.00
Small intestine weight g
0
10
20
30
40
Dose - μg
□ A2G-GLP-2(1-33)
△ L17K(3-(tetradecanoylamino)propionyl)/K30R-GLP-2(1-33)
○ L17K(3-(hexadecanoylamino)propionyl)/K30R-GLP-2(1-33)
2.00
1.75
1.50
1.25
1.00
Small intestinal weight g
-1.5
-1.0
-0.5
0.0
0.5
1.0
1.5
2.0
log(Dose)
□ A2G-GLP-2(1-33)
△ L17K(3-(tetradecanoylamino)propionyl)/K30R-GLP-2(1-33)
○ L17K(3-(hexadecanoylamino)propionyl)/K30R-GLP-2(1-33)

Figure 9.



A2G-GLP-2(1-33)

L17K(3-(tetradecanoylamino)propionyl)/K30R-GLP-2(1-33)

L17K(3-(hexadecanoylamino)propionyl)/K30R-GLP-2(1-33)

Figure 10.

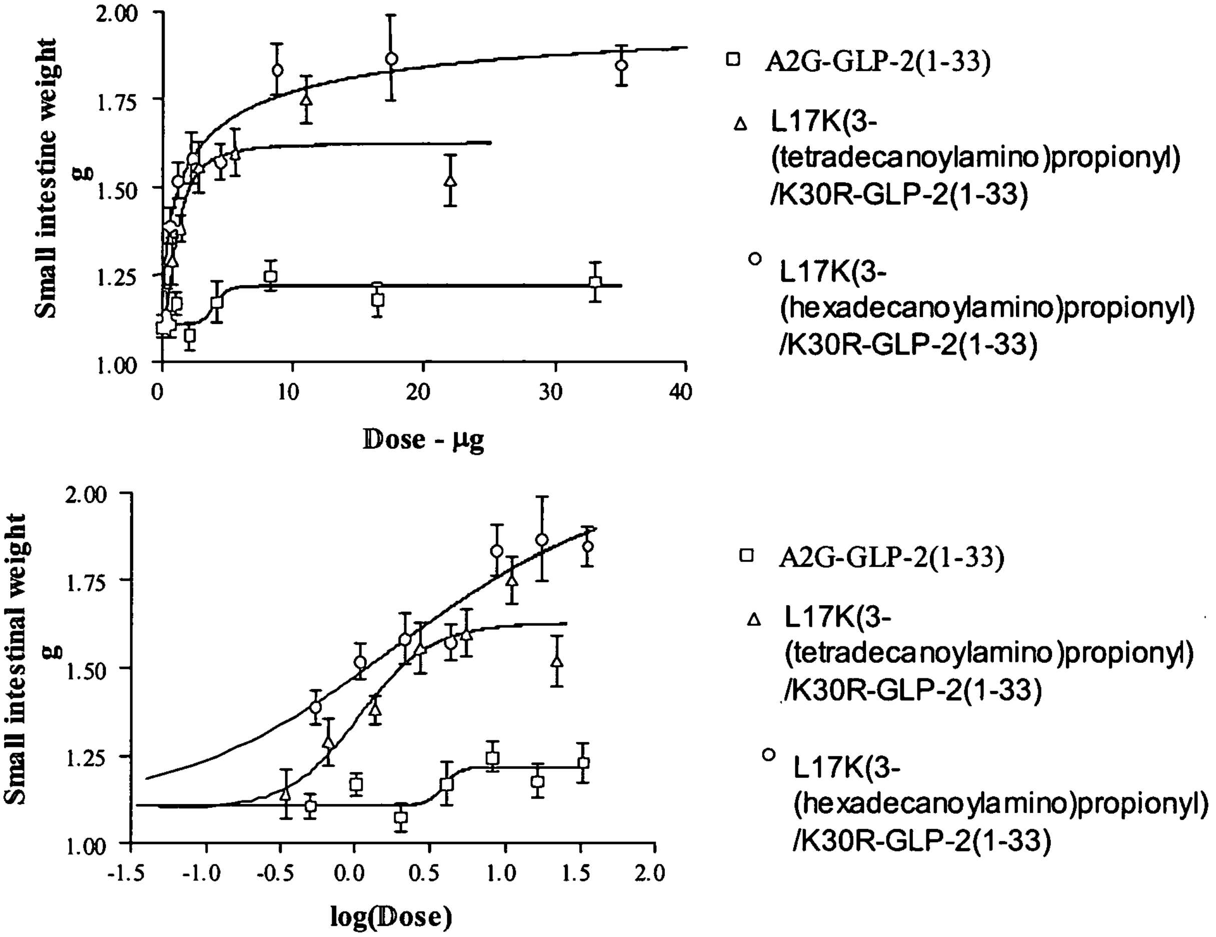
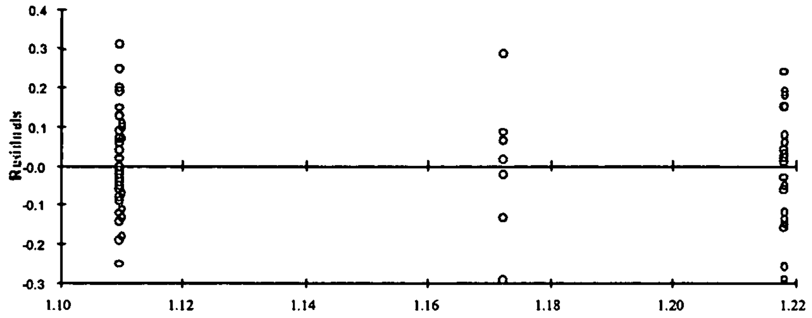
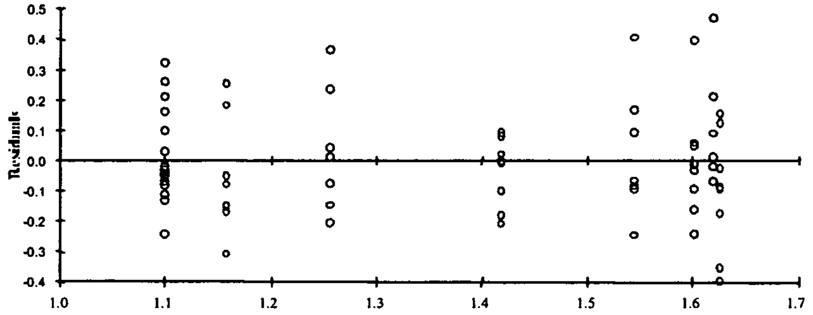

2.00
1.75
1.50
1.25
1.00
Small intestine weight g
0
10
20
30
40
Dose - μg
☐ A2G-GLP-2(1-33)
△ L17K(3-(tetradecanoylamino)propionyl)/K30R-GLP-2(1-33)
○ L17K(3-(hexadecanoylamino)propionyl)/K30R-GLP-2(1-33)
2.00
1.75
1.50
1.25
1.00
Small intestinal weight g
-1.5
-1.0
-0.5
0.0
0.5
1.0
1.5
2.0
log(Dose)
☐ A2G-GLP-2(1-33)
△ L17K(3-(tetradecanoylamino)propionyl)/K30R-GLP-2(1-33)
○ L17K(3-(hexadecanoylamino)propionyl)/K30R-GLP-2(1-33)

Figure 11.

A2G-GLP-2(1-33)



L17K(3-(tetradecanoylamino)propionyl)/K30R-GLP-2(1-33)



L17K(3-(hexadecanoylamino)propionyl)/K30R-GLP-2(1-33)

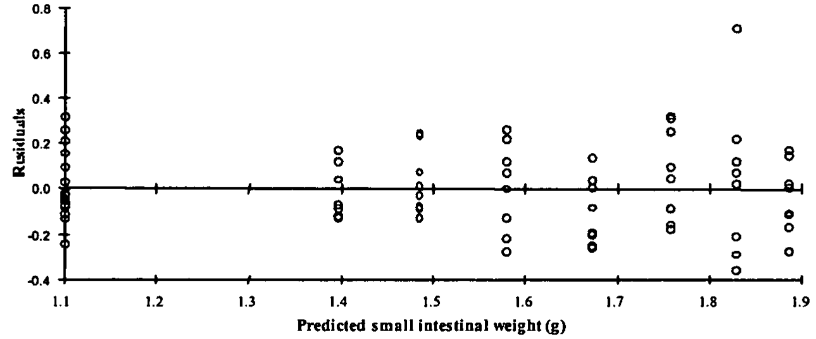


Figure 12.

SEQ ID NO. 1 (The amino acid sequence of native human GLP-2):

H A D G S F S D E M N T I L D N L A A R D F I N W L I Q T K I T D

SEQ ID NO. 2 (GLP-2 peptides according to formula I):

His-X^2-X^3-Gly-X^5-Phe-X^7-X^8-X^9-X^{10}-X^{11}-X^{12}-X^{13}-X^{14}-X^{15}-X^{16}-X^{17}-X^{18}-Ala-Arg-X^{21}-Phe-Ile-X^{24}-Trp-Leu-Ile-X^{28}-Thr-Arg-Ile-Thr-X^{33}

wherein X^2 is Ala, Val or Gly; X^3 is Asp, or Glu; X^5 is Ser, or Lys; X^7 is Ser, or Lys; X^8 is Asp, Glu, or Lys; X^9 is Asp, Glu, or Lys; X^{10} is Met, Lys, Leu, Ile, or Nor-Leucine; X^{11} is Asn, or Lys; X^{12} is Thr, or Lys; X^{13} is Ile, or Lys; X^{14} is Leu, or Lys; X^{15} is Asp, or Lys; X^{16} is Asn, or Lys; X^{17} is Leu, or Lys; X^{18} is Ala, or Lys; X^{21} is Asp, or Lys; X^{24} is Asn, or Lys; X^{28} is Gln, or Lys; X^{33} is Asp, Glu, or Lys.

SEQ ID NO. 3 (GLP-2 peptides according to formula II):

His-X^2-X^3-Gly-X^5-Phe-X^7-X^8-X^9-X^{10}-X^{11}-X^{12}-X^{13}-X^{14}-X^{15}-X^{16}-X^{17}-X^{18}-Ala-X^{20}-X^{21}-Phe-Ile-X^{24}-Trp-Leu-Ile-X^{28}-Thr-X^{30}-Ile-Thr-X^{33}

wherein X^2 is Ala, Val or Gly; X^3 is Asp, or Glu; X^5 is Ser, or Lys; X^7 is Ser, or Lys; X^8 is Asp, Glu, or Lys; X^9 is Asp, Glu, or Lys; X^{10} is Met, Lys, Leu, Ile, or Nor-Leucine; X^{11} is Asn, or Lys; X^{12} is Thr, or Lys; X^{13} is Ile, or Lys; X^{14} is Leu, or Lys; X^{15} is Asp, or Lys; X^{16} is Asn, or Lys; X^{17} is Leu, or Lys; X^{18} is Ala, or Lys; X^{20} is Arg, or Lys; X^{21} is Asp, or Lys; X^{24} is Asn, or Lys; X^{28} is Gln, or Lys; X^{30} is Arg, or Lys; X^{33} is Asp, Glu, or Lys.